UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Note to Reader
January 15, 1998

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack E. Housenger, Acting Director
Special Review and Reregistration Division

10/28/98

MEMORANDUM

Subject: **Ethyl Parathion.** Dietary and Occupational Risk Assessments
PC Code: 057501
Reregistration Case No: 0155

From: Richard Griffin
Reregistration Branch II
Health Effects Division (7509C)

Through: Alan Nielsen, Branch Senior Scientist
Reregistration Branch II
Health Effects Division

To: William Sproat
Reregistration Branch I
Special Review and Reregistration Division (7508W)

This memorandum summarizes the Health Effects Division review of residue chemistry, toxicology, and exposure data submitted to support the reregistration of ethyl parathion and provides risk assessments for dietary and occupational exposure. The dietary risk assessment will be revised following the review of recently submitted ruminant and poultry magnitude of the residue data. Analysis of these data may alter the estimates for ethyl parathion residues used to determine dietary risk from meat, milk, poultry, and eggs. Also, this assessment does not address the concern that ethyl parathion exposure may occur due to residues in/on imported commodities, as indicated by recent data. The following attachments provide the detailed information and conclusions on which the dietary and occupational risk assessments are based:

Ethyl Parathion - Report of the Hazard Identification Assessment Review Committee (N. Paquette/J. Rowland, 3/25/98)

Parathion. The Outcome of the HED Metabolism Assessment Review Committee Meeting Held on March 11, 1998 (B. Cropp-Kohlligian, 5/21/98)

Residue Chemistry Chapter for the Parathion Reregistration Eligibility (RED) Document (B. Cropp-Kohlligian, 5/27/98)

Parathion Reregistration. Anticipated Residue Estimates Based on Available Monitoring Data (B. Cropp-Kohlligian, 9/10/98)

Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document for Ethyl Parathion (J. Becker, 5/21/98)

Review of Parathion Incident Reports (J. Blondell, 3/30/98)

Also attached are Dietary Exposure Evaluation Model (DEEM) summary tables.

Executive Summary:

Ethyl parathion, also commonly known as parathion, is an acutely toxic insecticide currently registered for use on alfalfa, barley, wheat, corn, cotton, sorghum, soybean, sunflowers, and canola. The Agency considers the toxicological database to be adequate for reregistration and has established endpoints for risk assessment based on the critical toxic effect of cholinesterase inhibition. Based on the current level of refinement for anticipated residue estimates and uncertainties for dietary exposure to ethyl parathion from imported commodities, the Agency cannot conclude that ethyl parathion exposure via food sources is less than the level determined to have no adverse effect. Ethyl parathion is a restricted use pesticide limited to agricultural use only. Residential exposure is excluded from consideration in the aggregate risk assessment. Drinking water is excluded from aggregate risk assessment at this point since the dietary risk estimates, based on food sources only, greatly exceed the established chronic and acute Reference Doses. The aggregate risk assessment considering both food and drinking water exposure will be completed once the dietary risk assessment based on foods is less than the established acute and chronic Reference Doses. Similarly, although the Agency has made assumptions of maximum mitigation of worker risk by known means, the Agency cannot conclude that ethyl parathion exposure to workers at application and post-application is less than the level determined to have no adverse effect.

Ethyl parathion is currently formulated with methyl parathion, also a cholinesterase-inhibiting organophosphate. Experiments have shown that certain cholinesterase-inhibiting pesticides, when administered to test animals, are more toxic than the sum of their individual toxicities (40 CFR 180.35 Tests for Potentiation). At this time, it is unknown whether potentiation would occur following exposure to this multiple active ingredient (MAI) formulation. The potential for potentiation, or any other interaction, may need to be addressed at a later date. Cumulative risk assessment, considering other pesticides with a common mechanism of effect

(cholinesterase inhibition), is not addressed in this memorandum.

Background

Ethyl parathion [*0,0*-diethyl *0-p*-nitrophenyl thiophosphate] is an organophosphorus insecticide/miticide currently registered for use on alfalfa, barley, corn, cotton, canola, sorghum, soybean, sunflower, and wheat. All technical ethyl parathion sold in the United States is manufactured by Cheminova Agro A/S and is formulated solely as an emulsifiable concentrate.

In 1991 the Agency, and most of the registrants of products containing ethyl parathion, reached an agreement (*Federal Register Notices Vol. 56, No. 240 dated 11/13/91; and Vol. 57, No. 19 dated 1/29/92 and No. 34 dated 2/20/92)* under which the registrants agreed to limit sites and to restrict the application and post-application practices for ethyl parathion. This action was taken by the Agency to mitigate what was considered an *unreasonable* risk to workers exposed during application and post-application. Since the agreement, ethyl parathion use has been restricted to the crops listed above, and worker exposure has been partially mitigated by label restrictions including aerial-only application, mechanical-only harvesting, and other more restrictive requirements for protective clothing and handling.

The OPP Biological and Economic Analysis Division (BEAD) estimates that the yearly average for total U.S. ethyl parathion use is approximately 800,000 lbs. active ingredient (a.i.) with an estimated upper limit of approximately 1,100,000 lbs a.i./year (D. Brassard memo, 6/3/98). Total yearly use may vary according to pest pressure. For risk assessment, BEAD has provided the following estimates of percent of total acres per crop that treated with ethyl parathion: Alfalfa; 1%, Barley; 0.7%, Wheat; 1.3%, Field Corn; 0.01%, Sweet Corn; 8%, Cotton; 2%, Sorghum; 2%, Soybean; 0.8%, Sunflower; 6%, and Canola; 3%.

Hazard Identification

Ethyl Parathion is among the most highly toxic organophosphorus insecticide registered and is a potent inhibitor of acetylcholinesterase (AchE). Dose related inhibition of plasma, red blood cell (RBC) and brain cholinesterase is the critical toxic effect and occurs in dogs and rats by all routes and following acute, subchronic and chronic exposures to relatively low doses. As with all sulfur-containing organophosphates, to produce toxicity, ethyl parathion must first undergo metabolic activation to its biological active oxygen analog, paraoxon. Acute lethality occurs in mammals at low doses regardless of route of exposure (See Table I). In animal studies, females are more sensitive than males to the toxic effects and lethality. Symptoms leading up to death are consistent with cholinergic overstimulation and include, headache, weakness, blurred vision, pin-point pupils, sweating, watering of eyes, drooling or frothing of the mouth, vomiting, tightness in the chest, labored breathing, muscle spasms, convulsions and coma. Death is primarily due to respiratory arrest from paralysis of the respiratory muscles.

Subchronic and chronic toxicity studies in rats and dogs indicate that cholinesterase

inhibition is the critical toxic effect and dogs are the most sensitive species. In a subchronic dietary study, apart from the cholinergic effects, female rats fed 3.75 mg/kg of ethyl parathion for 13 weeks had increased mortality rates and decreased body weights and male rats fed 1.25 and 3.75 mg/kg had decreased body weights. In a 2 year chronic study, female rats given 2.5 mg/kg had a higher mortality rate, developed anemia and retinal atrophy and degeneration and male rats developed severe myelin sheath degeneration of the sciatic nerve. In the subchronic and chronic studies in dogs there was no evidence of similar neuropathology, although plasma, RBC and brain cholinesterase activity were inhibited at relatively low doses.

Acute Toxicity of Ethyl Parathion

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
81-1	Acute Oral-Rat	243412	LD_{50} = 2.7 mg/kg, ♀ LD_{50} = 10.8 mg/kg ♂,	I
81-2	Acute Dermal-Rabbits	Literature[1]	LD_{50} = 6.8 mg/kg	I
81-3	Acute Inhalation	Literature[2]	LC_{50} = 0.084 mg/L	II
81-4	Primary Eye Irritation	HED Doc # 3999	Data requirement waived I63.81-4	
81-5	Primary Skin Irritation	HED Doc # 3999	Data requirement waived I63.81-3	
81-6	Dermal Sensitization	43439110	Not a Sensitizer	
81-8	Acute Neurotoxicity	43117901	Neurotox: NOEL = 2.5 mg/kg ♂ 0.5 mg/kg ♀ LOEL = 10.0 mg/kg ♂ 2.5 mg/kg ♀ based on FOB changes at 4 hrs post dose: DEATH occurred in males at 10.0 mg/kg	

The metabolism of ethyl parathion involves an oxidative desulfuration step (that

[1] Ware, George. *The Pesticide Book*, 1989, Thomson Publication, Fresno CA. P. 305

[2] HSDB 1998. Hazard Substances Data Bank. MEDLARS online Information Retrieval System. National Library of Medicine.

significantly enhances the anticholinesterase properties) to its oxygen analog, paraoxon. Further oxidative 0-deethylation occurs to produce hydrolysis products which are excreted almost entirely in the urine.

The HED Metabolism Assessment Review Committee concluded (B. Cropp-Kohlligian, 5/21/98) that ethyl parathion (parent), the metabolite *0,0*-diethyl-*0*-*p*-nitrophenyl phosphate (paraoxon), and the metabolite *0,0*-diethyl-*0*-4-acetamidophenyl phosphate (4-acetamidoparaoxon) are the residues of concern for risk assessment based on cholinesterase inhibition. Lacking toxicology data specific to 4-acetamidoparaoxon, the Agency assumes cholinesterase inhibiting properties equivalent to ethyl parathion parent.

In 1991, the HED Carcinogenicity Peer Review Committee reevaluated the carcinogenic classification of ethyl parathion. Ethyl parathion is classified as a Group C (possible human carcinogen) based on increased adrenal cortical tumors in male and female Osborne-Mendel rats and possible trends for thyroid follicular adenomas and pancreatic isle cell carcinomas in male rats. The Committee recommended that quantified risk assessment be based on the Reference Dose, which is based on non-carcinogenic effects. The RfD method will adequately account for chronic toxicity effects, including carcinogenicity since doses eliciting cholinesterase inhibition are significantly below those eliciting the carcinogenic effects summarized above.

Considerations for special sensitivity in infants and children (FQPA)

To address the Food Quality Protection Act (FQPA) requirement for an additional safety factor to protect infants and children, the HED Hazard Identification Assessment Review Committee (HIARC) reviewed the ethyl parathion toxicity database for evidence of neuropathology. Evidence of neuropathology may indicate an increased susceptability of the developing nervous system to ethyl parathion. Also examined for indications of enhanced sensitivity were prenatal developmental toxicity studies in rabbits and rats, and a two-generation reproduction study in rats.

The HIARC concluded (N. Paquette, 3/25/98) that ethyl parathion did not demonstrate a delayed neurotoxicity in the hen or other evidence of neuropathology. In the rabbit developmental study there were no treatment related effects on fetal weight, and no external or internal malformations observed. In the rat developmental study there were no treatment related effects on any parameters measured on fetuses and no internal or external malformations were observed. In the two-generation reproduction study in rats there was no treatment related reproductive toxicity in either generation throughout the study (although cholinesterase activity was not measured in offspring in this study). The HIARC Committee also concluded that, based on the data from the developmental toxicity study in rats, a developmental neurotoxicity study with ethyl parathion is not required and there are no significant uncertainties in the assessment of functional development following pre-and/or postnatal exposure.

Based on the weight-of-evidence of all available studies, the HIARC Committee

concluded that there was no increased susceptibility to rat or rabbit fetuses following in utero exposure or to pups following post natal exposure to ethyl parathion. Based on the data summarized above, the Committee also recommended in the *Comprehensive Review of the Organophosphates* (June 4, 1998) that the 10x FQPA safety factor be removed from both the chronic and acute Reference Doses. This recommendation was confirmed in HED's FQPA Safety Factor Recommendations (Combined Report of the HIARC and Safety Factor Committee and its Recommendations for the Organophosphates) dated 8/6/98.

Endpoints / doses for risk assessment:

Dietary

Acute Reference Dose: The Agency has established an *acute* Reference Dose (RfD) of 0.00025 mg/kg body weight/day to assess the risk associated with a single oral exposure (single-day food consumption estimates in this assessment) to ethyl parathion. The acute RfD is based on plasma and RBC cholinesterase inhibition in an acute neurotoxicity study in rats (MRID 43117901). In this study neurobehavioral and neuropathological effects, plasma, RBC, and brain cholinesterase were determined. This study is appropriate for use in acute dietary risk assessment since the endpoint of cholinesterase inhibition was measured 4 hours after a single oral dose (exposure period of concern) on the day of treatment.

Based on the results of this study, the plasma and RBC cholinesterase inhibition No Observed Effect Level (NOEL) is 0.025 mg/kg for both males and females, and the Lowest Observed Effect Level (LOEL) is 2.5 mg/kg for males and 0.5 mg/kg for females. The neurobehavioral NOEL is 2.5 mg/kg for males and 0.5 mg/kg for females, with abnormal FOB and clinical signs of cholinergic toxicity evidenced at the LOEL of 10 mg/kg for males and 2.5 mg/kg for females. The brain cholinesterse inhibition LOEL was 10 mg/kg for males and 2.5 mg/kg for females.

An uncertainty factor of 100 was determined for the ethyl parathion acute RfD based on 10x for interspecies extrapolation and 10x for intraspecies variation.

Chronic Reference Dose: The Agency has established a *chronic* Reference Dose of 0.000033 mg/kg body weight/day to assess the risk associated with long-term dietary exposure to ethyl parathion. The chronic RfD is based on plasma and RBC cholinesterase inhibition in a one-year feeding study in dogs (MRID 24664243).

Dose-related decreases in plasma and RBC cholinesterase activity were observed at all dose levels in both male and female dogs. Brain cholinesterase was statistically significantly reduced only in females, in the mid-dose group. The LOEL was 0.01 mg/kg (LDT) based on decreased plasma and RBC cholinesterase in both males and females. A NOEL for plasma/RBC cholinesterase inhibition was not established in this study.

The RfD is based on the LOEL of 0.01 mg/kg and an uncertainty factor of 300. The uncertainty factor is based on 10x for interspecies extrapolation, 10x for intraspecies variation, and an additional factor of 3 to account for the lack of a NOEL.

Occupational:

Inhalation and Dermal Absorption: Inhalation and dermal risk estimates are based on an assumption of 100 percent absorption. This assumption is supported by the oral LD_{50}, dermal $LD_{50,}$ and inhalation LC_{50} studies which demonstrated toxicity at similar doses in multiple species via all routes of exposure (summarized above in hazard identification).

Inhalation Exposure: Based on the high acute toxicity (LC_{50}=0.084 mg/L) shown in a rat study, and use patterns of up to 1 lb. a.i./acre, there is considerable concern for occupational inhalation exposure to ethyl parathion. Inhalation of ethyl parathion vapor or aerosol leads to rapid absorption with imminent risk of respiratory failure. The HIARC concluded that inhalation exposure estimates (in ug a.i./day) should be converted to an equivalent of an oral dose (in mg/kg/day), aggregated with the dermal exposure estimate (also converted to an oral equivalent) and the resulting sum compared to the short and/or intermediate (oral) doses designated for occupational risk assessment.

Short-Term: Risk estimates for short-term (1-7 day) combined dermal and inhalation occupational exposure to ethyl parathion are based on the dose (NOEL) of 0.025 mg/kg body weight/day established in the rat *oral* acute neurotoxicity study (MRID 43117901) which demonstrated plasma, RBC, and brain cholinesterase inhibition. This study is summarized above as the basis of the acute oral RfD. Exposure estimates are compared to the dose of 0.025 mg/kg/day with risk expressed as a Margin of Exposure (the ratio of exposure to dose). The Agency considers an estimated Margin of Exposure (MOE) of 100 to be adequately protective for this risk assessment.

Intermediate-Term: Risk estimates for intermediate-term (7 days to several months) combined dermal and inhalation occupational exposure to ethyl parathion are based on plasma cholinesterase inhibition in a 6-month *oral* toxicity study in dogs. The study NOEL was determined to be 0.0024 mg/kg body weight/day based on the markedly reduced plasma cholinesterase in both males and females observed by Week 6 and throughout the study at 0.079 mg/kg/day (study LOEL). Exposure estimates are compared to the dose of 0.0024 mg/kg/day with risk expressed as a Margin of Exposure. The Agency considers a MOE of 100 to be adequately protective for this risk assessment.

Chronic: The HIARC concluded that, based on current use patterns for ethyl parathion (2-6 applications/season with 5-7 day intervals) there is likely no worker exposure of the duration considered long-term (several months to life-time) and this risk assessment can be excluded.

SUMMARY OF TOXICOLOGY ENDPOINT SELECTION

The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary Female 13+, Infants and Children, Adult Male	NOEL=0.025 UF = 100	Plasma and RBC ChE Inhibition in both male and female rats	Acute Oral Neurotoxicity in Rats
	Acute RfD = 0.00025 mg/kg/day		
Chronic Dietary	LOEL=0.01 UF = 300	Plasma and RBC ChE Inhibition in both male and female dogs	Chronic Toxicity - Dog
		Chronic RfD = 0.000033 mg/kg/day	
Short-Term (Dermal)	Oral NOEL=0.025	Plasma and RBC ChE Inhibition in both male and female rats	Acute Oral Neurotoxicity in Rats
Intermediate-Term (Dermal)	Oral NOEL=0.0024	Plasma and RBC ChE Inhibition in both male and female dogs	6 Month Oral Toxicity -Dog
Long-Term (Dermal)	None	The use pattern and exposure scenario does not indicate a need for long term risk assessment	
Short Term (Inhalation [3])	Oral NOEL= 0.025	Plasma & RBC ChE Inhibition	Acute Neurotoxicity in Rats
Intermediate Term (Inhalation [1])	Oral NOEL=0.0024	Plasma & RBC ChE Inhibition	6 Month Oral Toxicity-Dog
Long Term (Inhalation)	NONE	The use pattern and exposure scenario does not indicate a need for long term risk assessment	

Non-Occupational (Aggregate) Exposure and Risk Estimates:

[3] Appropriate route-to-route extrapolation should be performed for these risk assessments (i.e. dermal and inhalation exposure components using absorption rates of 100% for both) should be converted to equivalent oral doses and compared to the oral NOELs.

Dietary Exposure Data (Foods Only):

The HED Metabolism Assessment Review Committee (memo by B. Cropp-Kohlligian dated 5/21/98) has concluded that ethyl parathion residues of concern in plant commodities include ethyl parathion, its metabolite paraoxon [*O,O*-diethyl-*O*-*p*-nitrophenyl phosphate], and *p*-nitrophenol and that ethyl parathion residues of concern in animal commodities include ethyl parathion, paraoxon, *p*-nitrophenol, and 4-acetamidoparaoxon. The tolerance expression for plant and animal commodities will be based on ethyl parathion only. Ethyl parathion residues of concern to be included in the risk assessment for plant commodities will include ethyl parathion and paraoxon. Ethyl parathion residues of concern to be included in the risk assessment for animal commodities will include ethyl parathion, paraoxon, and 4-acetamidoparaoxon. Residues of *p*-nitrophenol resulting from the use of ethyl parathion do not have to be included in the tolerance expression or considered in the aggregate risk assessment for ethyl parathion, but should be considered in conjunction with the cumulative risk assessment for *p*-nitrophenol.

Tolerances for residues of ethyl parathion or its methyl homolog (methyl parathion) in/on numerous raw agricultural commodities (RACs) have been established under 40 CFR §180.121(a) and §180.319. No tolerances for residues of ethyl parathion have been established for animal commodities or processed food/feed commodities. Although tolerances for residues of ethyl parathion are currently expressed in terms of ethyl parathion or its methyl homolog (methyl parathion) [40 CFR §180.121 (a) and §180.319], the Agency has recommended that tolerances for ethyl parathion should be moved from 40 CFR §180.121(a) and listed under a separate 40 CFR §180.XXX (a) section. Under the new listing, tolerances should only be established for RACs and, if necessary, processed commodities of alfalfa, barley, canola, corn, cotton, grain sorghum, soybean, sunflower, and wheat, in accordance with an agreement limiting the use of ethyl parathion to these crops. All other currently established tolerances for residues of ethyl parathion listed under 40 CFR §180.121 (a) and §180.319 should be revoked.

The tolerance definition for ethyl parathion residues should also be changed to read as follows: *Tolerances are established for the residues of ethyl parathion [O,O-diethyl-O-p-nitrophenyl thiophosphate] in/on the following raw agricultural commodities:*

Although Cheminova Agro A/S has not indicated that they will support any uses of ethyl parathion other than those on alfalfa, barley, corn, cotton, canola, sorghum, soybean, sunflower, and wheat, the need to retain tolerances for residues of ethyl parathion in/on imported commodities such as fruits and vegetables has not been adequately addressed. The potential need for import tolerances on some fruits and vegetables is evident since Codex MRLs for residues of ethyl parathion are currently established on fruits and vegetables (0.5 ppm to 1 ppm) and recent PDP and FDA monitoring data (1996) have identified residues of ethyl parathion in/on some imported fruits and vegetables such as grapes and carrots.

The qualitative nature of the residue in plants is adequately understood based on cotton,

potato and wheat metabolism studies and the qualitative nature of the residue in animals is adequately understood based on acceptable ruminant and poultry metabolism studies.

Adequate analytical methodology is available for data collection and for the enforcement of ethyl parathion tolerances in plant commodities. However, if recently submitted feeding studies indicate that tolerances are necessary for ethyl parathion residues in animal commodities, then enforcement methods will be required for determining ethyl parathion residues in animal commodities. FDA multiresidue methods provide complete recovery of ethyl parathion and paraoxon.

Reregistration data requirements for magnitude of the residue in/on plants are fulfilled for the following crops/commodities: canola, corn, cottonseed, grain sorghum, soybean hay, soybean seed, and sunflower. Adequate processing data are available for canola, corn, cottonseed, grain sorghum, and wheat. The available wheat grain processing data will be translated to the processed commodities of barley grain.

Additional magnitude of the residue data are required on the following commodities: alfalfa forage, alfalfa hay, aspirated grain fractions, barley grain, barley hay, barley straw, cotton gin byproducts, soybean forage, wheat grain, wheat forage, wheat hay, and wheat straw. Additional processing data are required to determine the potential for concentration of ethyl parathion residues of concern in soybean processed commodities and refined sunflower seed oil. Livestock feeding studies are also required.

Recently submitted barley hay, grain, and straw data, wheat grain and aspirated grain fractions data, sunflower seed and sunflower seed processing data, corn grain and aspirated grain fractions data, cottonseed and cotton gin byproducts data, and sorghum grain and aspirated grain fractions data are currently under review. Livestock feeding studies have also been submitted and once these data are reviewed, the need for tolerances for residues of ethyl parathion in animal commodities will be determined.

Residue Estimates for DietaryRisk Assessment (Food Only):

Refinements to the chronic dietary risk assessment have been made using percent crop treated data (D. Brassard memo, 6/3/98), available FDA and PDP monitoring data for soybeans, corn (pop and grain), flour, wheat, and barley (translation of monitoring data from wheat to barley), and available processing data. Refinements to the acute dietary risk assessment have been made using available FDA and PDP monitoring data for soybeans, corn (pop and grain), flour, wheat, and barley (translation of monitoring data from wheat to barley) and available processing data. Anticipated residue estimates used in the chronic and acute risk assessments for sorghum, cottonseed oil, cottonseed meal, canola oil, and sunflower seed oil are based on magnitude of the residue data including available processing data and are refined in the chronic dietary risk assessment to include percent crop treated data. Anticipated residue estimates used in the chronic and acute risk assessments for meat, milk, poultry, and eggs are based on available

goat and hen metabolism data and are considered “upper end”.

As indicated earlier, the potential for dietary exposure to ethyl parathion residues of concern from imported commodities cannot be assessed until the issues surrounding the need for import tolerances for residues of parathion are resolved. Failure to include dietary exposure to ethyl parathion residues of concern from imported fruits and vegetables could constitute a significant underestimation in the dietary risk assessments. As an example of potential dietary risk concerns not currently addressed, the 1996 PDP monitoring program identified detectable residue of parathion in/on imported (washed) carrot samples (up to 0.007 ppm; 0.7% of carrot samples had detectable residues of parathion) and imported (washed with inedibles removed) grape samples (up to 0.021 ppm; 1.6% of grape samples had detectable residues of parathion). These findings are generally supported by data acquired in the 1995 PDP monitoring and 1995-1996 FDA monitoring programs.

Dietary Risk Estimates (Food Only):

The *Dietary Exposure Evaluation Model (DEEM)* software, based on 1989-92 USDA food consumption data, was used to estimate both acute and chronic dietary risk.

Acute Risk: The DEEM model was used to calculate acute dietary exposure estimates based on *total single-day* (rather than single-serving) consumption data. The following acute dietary risk estimates for ethyl parathion are considered Tier 1 (or upper-end) estimates since the commodity residue levels used are point estimates (also upper-end) rather than a distribution of residues, an upper-end consumption (95th percentile) estimate is used, and available percent crop treated information is *not* used. Based on the residue and consumption data outlined above, the DEEM program estimates that the “U.S. population - all seasons” and all DEEM population subgroups, including “All infants” are exposed to ethyl parathion at a level greater than 2,000 percent of the acute Reference Dose (see attached DEEM summary).

Chronic Risk: The DEEM model calculates chronic exposure estimates based on *averaged* consumption data for the average U.S. population and various population sub-groups including infants and children. Based on the residue and percent crop treated data outlined above, the DEEM program estimates that the “U.S. population - all seasons” and all population subgroups, including “All infants”’ are exposed to ethyl parathion at a level greater than 1,700 percent of the chronic Reference Dose.

The DEEM program estimates that the major contribution to the dietary risk calculation for ethyl parathion is attributable to milk and the only parathion residue of concern identified in milk is 4-acetamidoparaoxon. The dietary risk assessment will be readdressed after review of the recently submitted poultry and ruminant feeding studies. However, a preliminary evaluation of these data do not indicate that, once reviewed, the Agency will be able to make a finding that parathion exposure via food sources is less than the level determined to have no adverse effect.

Also, as indicated earlier, the potential for dietary exposure to ethyl parathion residues of

concern from imported commodities cannot be assessed until the issues surrounding the need for import tolerances for residues of parathion are resolved. Failure to include dietary exposure to parathion residues of concern from imported fruits and vegetables could constitute a significant underestimation in the dietary risk assessments.

Dietary / Drinking Water Exposure Data:

The Environmental Fate and Effects Division (EFED) has completed an assessment (A. Al-Mudallal memo, 4/9/98) for ethyl parathion concentrations in surface and ground water. Based on the highest annual usage rates (cotton and sorghum), the GENEEC surface water model estimated an acute concentration of 166 ug/L and a 56-day concentration of 23 ug/l. Based on the SCI-GROW model, the predicted concentration of ethyl parathion in shallow ground water is not likely to exceed 1.2 ug/l. Ethyl paraoxon is considered in this assessment although no specific paraoxon environmental fate data are available.

At this time however, the concentration estimates above will not be used as part of the required aggregate (non-occupational) risk assessement for ethyl parathion. Since the dietary risk estimates, based on food sources only, greatly exceed the established chronic and acute Reference Doses, HED does not consider it useful (at this point) to aggregate drinking water risk based on upper-end model estimates. Under current guidance HED calculates drinking water levels of comparison (DWLOC) based on the assumption that the risk estimate for food based and/or residential based exposure is less than the established Reference Doses.

Residential Exposure:

Ethyl parathion is a restricted use pesticide limited to agricultural use *only*. Residential exposure can be excluded from consideration in aggregate risk assessment.

Aggregate Risk Estimates:

Aggregate risk assessment, considering both food and drinking water exposure, was not calculated since the dietary risk estimates exceeded the acute and chronic Reference Doses.

Occupational Exposure and Risk Estimates:

Applicator Exposure:

Exposure Scenarios: Dermal and inhalation exposure can occur for those handling, loading, and applying ethyl parathion. Since the 1991 Agreement, handler and applicator exposure has been reduced by the following restrictions: 1) Aircraft loading must be by closed system with dry-couple shut-offs; 2) the loader cannot pilot the aircraft; 3) there must be an observer during loading to assist should an accident occur; and 4) human flaggers are prohibited.

Assumptions for Risk Assessment: Based on current use patterns, HED concludes that the likely exposure durations for ethyl parathion workers require risk assessments based on the endpoints and doses established for short-term (1 to 7 days) and intermediate-term (1 week to several months) intervals. HED has identified three major applicator scenarios relevant to exposure estimation: 1) mixing / loading for aerial application; 2) applicators (pilots) in fixed-wing aircraft; and 3) applicators (pilots) in helicopters. For risk assessment, an assumption is made that ethyl paration is being applied at the maximum labeled rate and that 350 acres will be treated in a single day. Dermal and inhalation absorption is expected to be 100 percent of exposure.

Risk Estimates: Based on the above assumptions, HED has calculated Margins of Exposure risk estimates for short-term and intermediate-term durations and has assumed mitigation by known engineering controls. The estimated MOEs for the above three scenarios are less than 10 (below the level of 100 considered adequate by the Agency). The use of risk mitigation measures for occupational handlers (i.e., maximum PPE and engineering controls) will not result in MOEs greater than 100 at the application rates supported by the registrant.

Postapplication Exposure:

Although the method of harvesting ethyl parathion treated fields is restricted to mechanical-only, post application dermal exposure can occur for workers entering fields for scouting and irrigating. Current labels restrict reentry for any reason for four hours, and state a Restricted Entry Interval (REI) of 3 days (6 days for corn). For this risk assessment, HED has selected one scenario to represent postapplication exposure. HED has used scouting in cotton to represent reasonable activities that would commonly occur in all of the 9 crops. The assessment is based on default transfer coefficient (Tc) values, assumes a one-hour exposure per day, and risk estimates are based on the dose selected for intermediate-term intervals.

Risk Estimates: Based on the above assumptions, HED has calculated that an interval of 62 to 69 days must occur before the estimated Margins of Exposure are 100, or greater.

Worker Incident Data:

Based on a recent review of ethyl parathion poisoning data (1992-1996) following the consent agreement, the following poisoning incidents have been reported (memo from Jerome Blondell (HED) to Jonathan Becker (HED), dated March 30, 1998): 1) Incident Data System (IDS) includes two incidents, one from Minnesota and one from South Dakota. Both were related to spray drift exposure. Systemic / health effects were not reported, and 2) California reported six incidents involving ethyl parathion in 1992 and no incidents from 1993 through 1996. Three incidents involved drift from a plum orchard related to misuse. The three other incidents related to handlers cleaning or working on spray rigs. This report concludes that a very small number of parathion cases have been reported since the settlement agreement of 1991, and for the incidents that are reported either spray drift or equipment maintenance are the principle sources of exposure.

Residential Postapplication Exposure: All labels include language concerning the maintenance of a buffer zone of 100 feet from buildings, public roads, or bodies of water to minimize the exposure via spray drift to bystanders. However, without actual exposure data, or validated modeling results, HED remains concerned that the existing buffer zones may not be not adequately protective and would not prevent ethyl parathion exposure to bystanders. The registrant is a member of the Spray Drift Task Force and HED reserves the decision concerning the magnitude of bystander spray drift exposure and the required buffer zone until data from the task force are evaluated.

DEEM DIETARY RISK SUMMARY TABLES

Residues for Acute Risk Assessment

FILENAME: D:\057501ac.R91 CHEMICAL NAME: Ethyl parathion
RfD(CHRONIC): .000033 mg/kg/DAY NOEL(CHRONIC): .010000 mg/kg/day
RfD(ACUTE): .000250 mg/kg/DAY NOEL(ACUTE): .025000 mg/kg/day Q*=.0000
Date created/last modified: 10-23-1998/08:53:11/8 Program ver. 6.16
Comment: Chronic RfD set on LOEL

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	#2	Comment
265	O	BARLEY	000.020000		01.000	01.000	
324	U	BEEF-FAT W/O BONES	000.110000		01.000	01.000	
325	U	BEEF-KIDNEY	000.500000		01.000	01.000	
326	U	BEEF-LIVER	000.800000		01.000	01.000	
327	U	BEEF-LEAN(FAT/FREE)W/O BONES	000.140000		01.000	01.000	
323	U	BEEF-DRIED	000.140000		01.920	01.000	
321	U	BEEF-MEAT BYPRODUCTS	000.140000		01.000	01.000	
301	A	CANOLA OIL (RAPE SEED OIL)	000.180000		01.500	01.000	
368	V	CHICKEN-FAT W/O BONES	000.010000		01.000	01.000	
369	V	CHICKEN-LEAN/FATFREE W/O BONE	000.003000		01.000	01.000	
367	V	CHICKEN-GIBLETS(LIVER)	000.002000		01.000	01.000	
366	V	CHICKEN-BYPRODUCTS	000.003000		01.000	01.000	
237	O	CORN/POP	000.006000		01.000	01.000	
267	O	CORN GRAIN-BRAN	000.006000		01.000	01.000	
268	O	CORN GRAIN/SUGAR/HFCS	000.006000		01.500	01.000	
266	O	CORN GRAIN-ENDOSPERM	000.006000		01.000	01.000	
238	O	CORN/SWEET	000.100000		01.000	01.000	
388	O	CORN GRAIN/SUGAR-MOLASSES	000.006000		01.500	01.000	
289	O	CORN GRAIN-OIL	000.020000		01.000	01.000	
290	A	COTTONSEED-OIL	000.015000		01.000	01.000	
291	A	COTTONSEED-MEAL	000.030000		01.000	01.000	
365	X	EGGS-YOLK ONLY	000.000080		01.000	01.000	
363	X	EGGS-WHOLE	000.000080		01.000	01.000	
364	X	EGGS-WHITE ONLY	000.000080		01.000	01.000	
319	X	MILK-FAT SOLIDS	000.200000		01.000	01.000	
398	X	MILK-BASED WATER	000.200000		01.000	01.000	
320	X	MILK SUGAR (LACTOSE)	000.200000		01.000	01.000	
318	X	MILK-NONFAT SOLIDS	000.200000		01.000	01.000	
362	V	POULTRY-OTHER-FAT W/O BONES	000.010000		01.000	01.000	
360	V	POULTRY-OTHER-LEAN (FAT FREE)	000.003000		01.000	01.000	
361	V	POULTRY-OTHER-GIBLETS(LIVER)	000.002000		01.000	01.000	
275	O	SORGHUM (INCLUDING MILO)	002.000000		01.000	01.000	
303	G	SOYBEAN-OTHER	000.006000		01.000	01.000	
307	G	SOYBEANS-FLOUR (DEFATTED)	000.006000		01.000	01.000	
305	G	SOYBEANS-FLOUR (FULL FAT)	000.006000		01.000	01.000	
297	G	SOYBEANS-OIL	000.006000		01.000	01.000	
304	G	SOYBEANS-MATURE SEEDS DRY	000.006000		01.000	01.000	
306	G	SOYBEANS-FLOUR (LOW FAT)	000.006000		01.000	01.000	
482	A	SOYBEANS-PROTEIN ISOLATE	000.006000		01.000	01.000	
417	A	SUNFLOWER-SEEDS	000.250000		01.000	01.000	
298	A	SUNFLOWER-OIL	000.250000		01.000	01.000	
357	V	TURKEY--FAT W/O BONES	000.010000		01.000	01.000	
356	V	TURKEY-GIBLETS (LIVER)	000.002000		01.000	01.000	
355	V	TURKEY-BYPRODUCTS	000.003000		01.000	01.000	
358	V	TURKEY-LEAN/FAT FREE W/O BONE	000.003000		01.000	01.000	
424	U	VEAL-FAT W/O BONES	000.110000		01.000	01.000	
425	U	VEAL-LEAN (FATFREE) W/O BONES	000.140000		01.000	01.000	
430	U	VEAL-MEAT BYPRODUCTS	000.140000		01.000	01.000	
426	U	VEAL-KIDNEY	000.500000		01.000	01.000	
427	U	VEAL-LIVER	000.800000		01.000	01.000	
429	U	VEAL-DRIED	000.140000		01.920	01.000	
277	O	WHEAT-GERM	000.020000		01.000	01.000	
278	O	WHEAT-BRAN	000.100000		01.000	01.000	
279	O	WHEAT-FLOUR	000.006000		01.000	01.000	
437	O	WHEAT-GERM OIL	000.020000		01.000	01.000	
276	O	WHEAT-ROUGH	000.020000		01.000	01.000	

Acute Dietary Risk Estimates

U.S. Environmental Protection Agency Ver. 6.27
DEEM ACUTE analysis for ETHYL PARATHION (1989-92 data)
Residue file name: 057501ac.R91 Adjustment factor #2 NOT used.
Analysis Date: 10-23-1998/08:56:53 Residue file dated: 10-23-1998/08:53:11/8
Acute Reference Dose (aRfD) = 0.000250 mg/kg body-wt/day
Run Comment: Chronic RfD set on LOEL

Summary calculations:

	95th Percentile		99th Percentile		99.9 Percentile	
	Exposure	% aRfD	Exposure	% aRfD	Exposure	% aRfD
U.S. pop - all seasons:	0.006067	2426.97	0.011156	4462.33	0.020271	8108.54
All infants (<1 year):	0.015020	6008.13	0.028661	>10000	0.038781	>10000
Children (1-6 years):	0.013164	5265.79	0.018735	7494.06	0.028221	>10000

Residues for Chronic Risk Assessment

FILENAME: D:\057501cr.R91 CHEMICAL NAME: Ethyl parathion
RfD(CHRONIC): .000033 mg/kg/DAY NOEL(CHRONIC): .010000 mg/kg/day
RfD(ACUTE): .000250 mg/kg/DAY NOEL(ACUTE): .025000 mg/kg/day Q*=.0000
Date created/last modified: 10-23-1998/08:52:05/8 Program ver. 6.16
Comment: Chronic RfD set on LOEL

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	#2	Comment
265	O	BARLEY	000.000300		01.000	01.000	
324	U	BEEF-FAT W/O BONES	000.110000		01.000	01.000	
325	U	BEEF-KIDNEY	000.500000		01.000	01.000	
326	U	BEEF-LIVER	000.800000		01.000	01.000	
327	U	BEEF-LEAN(FAT/FREE)W/O BONES	000.140000		01.000	01.000	
323	U	BEEF-DRIED	000.140000		01.920	01.000	
321	U	BEEF-MEAT BYPRODUCTS	000.140000		01.000	01.000	
301	A	CANOLA OIL (RAPE SEED OIL)	000.180000		01.500	00.030	
368	V	CHICKEN-FAT W/O BONES	000.010000		01.000	01.000	
369	V	CHICKEN-LEAN/FATFREE W/O BONE	000.003000		01.000	01.000	
367	V	CHICKEN-GIBLETS(LIVER)	000.002000		01.000	01.000	
366	V	CHICKEN-BYPRODUCTS	000.003000		01.000	01.000	
237	O	CORN/POP	000.000060		01.000	01.000	
267	O	CORN GRAIN-BRAN	000.000060		01.000	01.000	
268	O	CORN GRAIN/SUGAR/HFCS	000.000060		01.500	01.000	
266	O	CORN GRAIN-ENDOSPERM	000.000060		01.000	01.000	
238	O	CORN/SWEET	000.100000		01.000	00.080	
388	O	CORN GRAIN/SUGAR-MOLASSES	000.000060		01.500	01.000	
289	O	CORN GRAIN-OIL	000.000200		01.000	01.000	
290	A	COTTONSEED-OIL	000.015000		01.000	00.020	
291	A	COTTONSEED-MEAL	000.030000		01.000	00.020	
365	X	EGGS-YOLK ONLY	000.000080		01.000	01.000	
363	X	EGGS-WHOLE	000.000080		01.000	01.000	
364	X	EGGS-WHITE ONLY	000.000080		01.000	01.000	
319	X	MILK-FAT SOLIDS	000.200000		01.000	01.000	
398	X	MILK-BASED WATER	000.200000		01.000	01.000	
320	X	MILK SUGAR (LACTOSE)	000.200000		01.000	01.000	
318	X	MILK-NONFAT SOLIDS	000.200000		01.000	01.000	
362	V	POULTRY-OTHER-FAT W/O BONES	000.010000		01.000	01.000	
360	V	POULTRY-OTHER-LEAN (FAT FREE)	000.003000		01.000	01.000	
361	V	POULTRY-OTHER-GIBLETS(LIVER)	000.002000		01.000	01.000	
275	O	SORGHUM (INCLUDING MILO)	002.000000		01.000	00.020	
303	G	SOYBEAN-OTHER	000.000070		01.000	01.000	
307	G	SOYBEANS-FLOUR (DEFATTED)	000.000070		01.000	01.000	
305	G	SOYBEANS-FLOUR (FULL FAT)	000.000070		01.000	01.000	
297	G	SOYBEANS-OIL	000.000070		01.000	01.000	
304	G	SOYBEANS-MATURE SEEDS DRY	000.000070		01.000	01.000	
306	G	SOYBEANS-FLOUR (LOW FAT)	000.000070		01.000	01.000	
482	A	SOYBEANS-PROTEIN ISOLATE	000.000070		01.000	01.000	
417	A	SUNFLOWER-SEEDS	000.250000		01.000	00.060	
298	A	SUNFLOWER-OIL	000.250000		01.000	00.060	
357	V	TURKEY--FAT W/O BONES	000.010000		01.000	01.000	
356	V	TURKEY-GIBLETS (LIVER)	000.002000		01.000	01.000	
355	V	TURKEY-BYPRODUCTS	000.003000		01.000	01.000	
358	V	TURKEY-LEAN/FAT FREE W/O BONE	000.003000		01.000	01.000	
424	U	VEAL-FAT W/O BONES	000.110000		01.000	01.000	
425	U	VEAL-LEAN (FATFREE) W/O BONES	000.140000		01.000	01.000	
430	U	VEAL-MEAT BYPRODUCTS	000.140000		01.000	01.000	
426	U	VEAL-KIDNEY	000.500000		01.000	01.000	
427	U	VEAL-LIVER	000.800000		01.000	01.000	
429	U	VEAL-DRIED	000.140000		01.920	01.000	
277	O	WHEAT-GERM	000.000300		01.000	01.000	
278	O	WHEAT-BRAN	000.002000		01.000	01.000	
279	O	WHEAT-FLOUR	000.000200		01.000	01.000	
437	O	WHEAT-GERM OIL	000.000300		01.000	01.000	
276	O	WHEAT-ROUGH	000.000300		01.000	01.000	

Chronic Dietary Risk Estimates

U.S. Environmental Protection Agency Ver. 6.12
DEEM89N CHRONIC analysis for ETHYL PARATHION (1989-92 data)
Residue file name: 057501CR Adjustment factor #2 used.
Analysis Date 10-21-1998 Residue file dated: 10-21-1998/14:19:56/8
Reference dose (RfD, CHRONIC) = 0.000033 mg/kg body-wt/day
COMMENT 1: Chronic RfD set on LOEL

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Pop - 48 states - all seasons	0.001582	4,793.3%
U.S. Population - spring season	0.001578	4,780.5%
U.S. Population - summer season	0.001545	4,682.9%
U.S. Population - autumn season	0.001650	4,999.3%
U.S. Population - winter season	0.001555	4,710.9%
Northeast region	0.001573	4,766.4%
Midwest region	0.001790	5,424.3%
Southern region	0.001427	4,323.7%
Western region	0.001603	4,859.0%
Pacific Region	0.001591	4,820.1%
Hispanics	0.001728	5,235.5%
Non-hispanic whites	0.001591	4,822.7%
Non-hispanic blacks	0.001398	4,236.6%
Non-hispanic other than black or white	0.001676	5,078.9%
All infants (<1 year)	0.003014	9,132.2%
Nursing infants (<1 year)	0.000568	1,721.2%
Non-nursing infants (<1 year)	0.004043	12,251.3%
Children (1-6 years)	0.005652	17,127.1%
Children (7-12 years)	0.002944	8,922.3%
Females (13-19 yrs/not preg. or nursing)	0.001298	3,932.3%
Females (20+ years/not preg. or nursing)	0.000812	2,461.6%
Females (13-50 years)	0.000902	2,732.7%
Females (13+/pregnant/not nursing)	0.001498	4,540.1%
Females (13+/nursing)	0.001317	3,992.0%
Males (13-19 years)	0.001713	5,191.1%
Males (20+ years)	0.000849	2,572.2%
Seniors (55+)	0.000824	2,497.7%